RATE OF SECRETION OF THE PAROTID GLANDS IN NORMAL CHILDREN

A MEASUREMENT OF FUNCTION OF THE AUTONOMIC NERVOUS SYSTEM

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I. HISTORICAL BACKGROUND OF THE PROBLEM

The human salivary glands are among the most complex of all the glands of the body. They are relatively poorly understood, and many controversial issues have sprung up about their mechanisms, secretions and functions. The many inconsistencies in data in the literature are probably due in great part to the differences in technic which were used for the collection and study of their secretions. This is particularly true of the parotid glands. Therefore, the history of knowledge of the secretory reactions of the human parotid glands resolves itself to a large extent into a story of methodologic changes.

From 1832, when Mitscherlich [1] reported his first observations on human parotid secretion, till 1916 there were two methods used for the collection of isolated salivary secretions. These were direct collections from fistulas and collection by the use of cannulation. Six physicians who had patients with fistulas due to accidental cuts or burns did much of the pioneer work in the field. Starting with Mitscherlich, they were Stoney-Butler (1873),[2] Küss (1899),[3] Zebrowski (1904),[4] Smirnov (1921) [5] and Krasnogorski (1926).[6] There have been criticisms leveled at the fistula method on the basis that it involves a structural anomaly in

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1. Mitscherlich, C. G.: Ueber den Speichel des Menschen, Mag. f. d. ges. Heilk. **38**:491, 1832.

2. Stoney-Butler, P.: Effect of Stimuli on the Secretion of the Parotid Gland, J. Anat. & Physiol. **7**:161, 1873.

3. Küss, C.: Notes sur le salive parotienne de l'homme, J. de l'anat. et physiol. **35**:246, 1899.

4. Zebrowski, E.: Zur Frage der sekretorischen Funcktion der Parotis beim Menschen, Arch. f. d. ges. Physiol. **110**:105, 1925.

5. Smirnov, A. I.: The Secretion of the Parotid Gland in Man, Kubanski Nauchno-Med. Vestnik, 1921, nos. 2-4, p. 59.

6. Krasnogorski, N. I.: Ueber die Wirkung der Wärmereize auf die Tätigkeit der Speicheldrüsen bei Kindern, Monatschr. f. Kinderh. **42**:327, 1929.

which the conditions are possibly not applicable to normal functioning. However, even if this technic were reliable in investigations on human beings, subjects are too rare for extensive experimental work.

The first artificial method for collecting parotid secretions was devised in 1860 by Ordenstein,[7] who inserted a small cannula into the mouth of Stenson's duct. Besides being painful, this method proved too unreliable, since the duct expands under such stimulation, permitting the cannula to slip out or the secretions to leak past the cannula. Babkin [8] stated the belief that the cannula itself acts as an artificial stimulant to the gland. When Eckhard, in 1863,[9] and Oehl, in 1864,[10] used this method, they noted definite limitations; but when fairly recent studies,[11] quoted in the literature on the parotid glands, were made with cannulation these limitations were taken into consideration. The inaccuracies of data obtained in the latter experiments were pointed out by Korchin and Winsor.[12]

Studies on the human parotid glands received their greatest impetus with the discovery of a simple and ingenious device, a small suction and collection disk developed by Lashley in 1916.[13] This disk, the diameter of which is about that of a dime and which is about three times as thick, opened the door to a wealth of information on parotid activity in human beings. Without necessitating surgical treatment or subjecting the subjects to pain and discomfort, it made possible the most accurate measurements available of quantitative and qualitative variations in parotid secretion. Ten years later Krasnagorski created a similar device in Russia. His is the chief authoritative work dealing with the parotid secretions in children, its chief interest lying, however, in its treatment of the conditioned and unconditioned reflexes. Winsor's (1929) modification of Lashley's disk was used in compiling the figures on which this paper is based.

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7. Ordenstein, L.: Ueber den Parotidenspeichel des Menschen, Beitr. z. Anat. u. Physiol. **2**:103, 1860.

8. Babkin, B. P.: The Innervation of the Salivary Glands, Tr. Roy. Soc. Canad. (Sect. V. Biol. sc.) **25**:205, 1931.

9. Eckhard, G.: Ueber die Eigenschaften des Sekrets des menschlichen Glandula submaxillaris, Beitr. z. Anat. u. Physiol. **3**:39, 1863.

10. Oehl, E.: La saliva umana studiata colla siringazione dei condotti ghiandolari, Pavia, F. Fusi, 1864.

11. Clark, G. W., and Carter, K. L.: Factors Involved in Reaction Changes of Human Saliva, J. Biol. Chem. **73**:391, 1927.

12. Korchin, B., and Winsor, A. L.: The Relationship of Certain Organic Factors to Individual Differences in Human Parotid Secretory Rate, J. Exper. Psychol. **27**:192, 1940.

13. Lashley, K. S.: The Human Salivary Reflex and Its Use in Psychology, Psychol. Rev. **23**:446, 1916.

Richter and Wada [14] made a contribution to the method when they employed calibrated tubes for measuring the secretory rate. Prior to that time counting drops or determining the volume of saliva collected in test tubes or beakers was used.

There have been several modifications of the method originally used to hold the collecting disk in place in the mouth (Finesinger and Finesinger [15] and Jenness and Hackman [16]). Since the simplest suction method (Winsor and Strongin), described in the following pages, works satisfactorily, the more elaborate technic employed by those investigators has not been used in this study.

II. APPARATUS AND TECHNIC

The complete apparatus for collection and measurement of parotid secretion is called a sialometer. The disk used in these experiments consists of a silver-plated metal disk 14 mm. in diameter, out of which two concentric chambers are cut. The inner, or collecting, chamber is 10 mm. in diameter and 3 mm. deep. The outer chamber, in the form of a circular groove, is 1.5 mm. wide and 5 mm. deep (fig. 1). To provide for greater flexibility in conveying the secretion to the measuring device, rubber tubes of about the same bore are attached to the metal outlets from the chambers of the disks. The rubber tubing attached to the outer, or suction, chamber is about 45 cm. long. The tube which conveys the secretion from the inner chamber of the disk to the measuring device is long enough to extend loosely from the subject to the measuring device, which is situated in front of the experimenter.

The pipets are calibrated to 0.01 cc. Usually a 1 cc. pipet suffices in experiments on unstimulated rates. In order to avoid hydrostatic pressure, the level of the pipet is kept about 6 inches (15 cm.) below the level of the disk in the subject's mouth. It is not necessary to fill the entire collecting system with water or to wait till the saliva fills the tubing leading to the pipet. A 0.05 cc. bead of water in the pipet will be pushed along in the pipet by the column of air in the tubing as the gland secretes.

In use, a suction disk is placed against the inner surface of a cheek so that the central chamber covers the mouth of Stenson's duct. While the experimenter is looking for the opening of the duct he keeps the end of the short piece of rubber tubing in his mouth. As soon as the central chamber of the disk covers the opening of the duct, the experimenter can exhaust the air from the outer chamber of the disk by gently sucking the tube in his mouth. He then clamps off the tubing. The disk clings tightly to the check, and the secretion is free to flow into the central chamber and to push the column of water through the rubber tubes and recording device. It was found that elaborate suction pumps, bulbs and other methods of applying the suction were not as satisfactory as the simple method just described. Care is taken to avoid applying too much suction. (The suction is released at the end of the experimental period before the disks are removed.) The disks and

14. Richter, C. P., and Wada, T.: Method of Measuring Salivary Secretions in Human Beings, J. Lab. & Clin. Med. **9**:271, 1922.

15. Finesinger, J. E., and Finesinger, G. L.: Modification of Krasnogorski Method for Stimulating and Measuring Secretion from Parotid Glands in Human Beings, J. Lab. & Clin. Med. **22**:267, 1937.

16. Jenness, A., and Hackman, R. C.: Salivary Secretion During Hypnosis, J. Exper. Psychol. **22**:58, 1938.

rubber tubes and the hands of the experimenter are of course always carefully cleaned and sterilized before each experiment.

In order to avoid the factors of hunger or satiation—both of which affect the secretory activity of the glands—all crucial experiments are performed about one

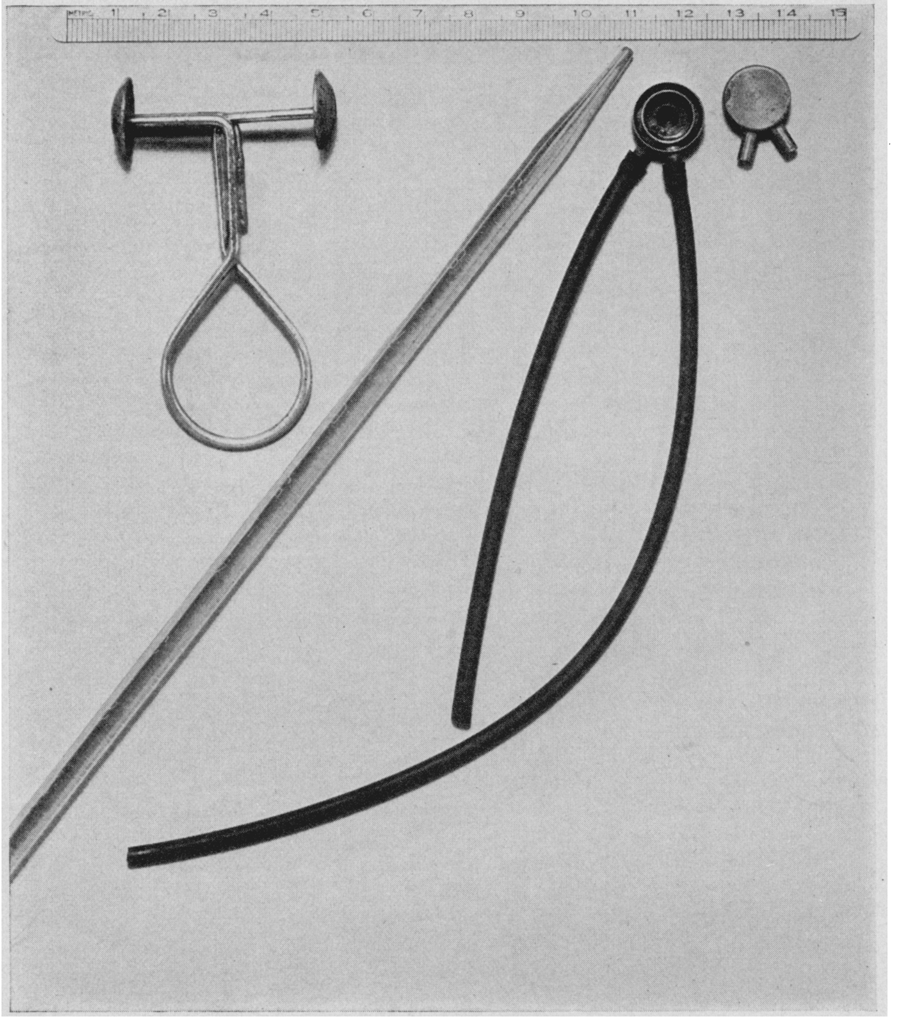

Fig. 1.—Apparatus for collection of saliva from the parotid glands.

and one-half to two hours after mealtimes. A consideration of the nature of the activation of the glands prior to an experiment or any part of an experiment is always imperative. In experiments which involve several changes in secretory activity time is allowed for the activity to return to normal before the next portion of the experiment is undertaken.

Attempts are made to put the subject at his ease and to accustom him to the laboratory situation. The child knows he will have a reward at the end of the "test." He is given one of the disks to play with, and he is encouraged to put it into his mouth to prove to himself that it is not painful. The apparatus is described to the subject, and its method of operation demonstrated. The subject is told that the disks should cause no discomfort at all. However, if too much suction is applied or if the disks are not placed directly over the openings of the ducts, the subject may experience some discomfort, in which event the disks are immediately removed. The subject is told before the onset of the experiment that if he experiences any pain or discomfort he shall inform the experimenter and the experiment will be terminated.

When applied correctly the collecting device itself does not affect the flow of secretion or seriously interfere with the oral movements of the subject. Experiments which had been performed on the effects of mechanical stimulation of the oral mucosa indicated that the effect of the presence of the disks on the secretory activity is negligible. The subject quickly becomes adapted to the presence of the disks and after a few minutes is usually quite comfortable. Even with disks on both parotid ducts the subject is able to converse and eat and drink in a normal fashion.

The subject is seated in front of a small table and is instructed to assume a comfortable posture. For records of a control, that is the secretory reaction in a condition without marked external stimulation, the subject is instructed to avoid excitatory movements of the tongue or throat, except as directed. In order that the accumulated secretions from the other salivary glands will not interfere with the subject's comfort, he is permitted to swallow at a given signal at the end of every five minute period when the control secretions are obtained. In view of the fact that swallowing increases the rate of flow, the secretion during the minute in which swallowing takes place is not included in the record of the control secretion. For the needs of the experiments reported in this paper the rate of flow was recorded every minute, accurately timed by means of a stopwatch.

To avoid the factor of dehydration (this is discussed more fully in part IV), if there is a suspicion of its presence clinically or in the history of intake and excretion of fluid, a McClure-Aldrich test is done (measuring the rate of absorption of 0.1 cc. of physiologic solution of sodium chloride injected intradermally).

The test period lasts twenty to thirty minutes (four to six periods of five minutes). No test is considered valid if it does not include three periods of five minutes.

A disk is applied to both the right and the left parotid duct whenever possible. The advantages of using both glands are many. It affords a check on the apparatus. A leak or other disturbance may be indicated if on stimulation only one of the glands responds normally. In addition, most persons have been found to have a certain amount of glandular dominance in parotid activity. Therefore, collection of secretions from both glands gives a truer picture of the average secretory activity. Collecting secretions from both sides also makes possible studies on organic neurologic problems which may eventually turn out to have some

implications in the localization of lesions of the brain of various types. These could not be investigated by the earlier method of using only one gland.

The isolation of the secretions from the other large salivary glands has not been satisfactorily accomplished thus far. Krasnagorski [17] and Gore (1937) have advocated the use of special suction disks which have not as yet been entirely adequate in actual use. Winsor and Korchin, after isolating the parotid secretions with disks as previously described, aspirated or had absorbed on tarred absorbent material (after Poth [18]) the secretions from the other glands, which could then be studied separately.

This investigation is concerned only with the unstimulated, inactivated or "resting" rate of parotid secretion. Therefore, my only contact with the large and important field of salivary stimulants has been with the use of lemon juice given at the onset of an experiment in those rare tests on children in whom there is no flow shortly after the disks are in place. This serves as a check on the correct application of the disks. At least five minutes must be allowed for the rate to become normal after a few drops of lemon juice is given. Some experiments are being carried on with olfactory stimuli which can be used to produce homolateral parotid activity (Ellsberg, Spotnitz and Strongin [19]). This is not in agreement with Lashley's [13] conclusion that "there is no direct reflex to olfactory . . . stimulation."

III. INNERVATION OF THE PAROTID GLANDS

Since this study has in its final analysis many implications in cortico-glandular relationships, it is felt that an outline of the probable neural connections of the parotid glands is worth while, especially in regard to their relations to the mechanisms of the autonomic nervous system.

The parotid glands are supplied by nerves derived from the parasympathetic and sympathetic nervous systems. Faradic stimulation of nerve cells at two definite points on the floor of the medulla oblongata on one side produces secretion from the ipsilateral salivary glands. Anatomic investigation by Kohnstamm,[20] Yagita and Hayama,[21] and the

17. Krasnogorski, N. I.: Bedingte und unbedingte Reflexe im Kindesalter und ihre Bedeutung für die Klinik, Ergebn. d. inn. Med. u. Kinderh. **39**:613, 1931.

18. Poth, E. J.: Simplified Technic for Quantitative Collection of Saliva from Man, Proc. Soc. Exper. Biol. & Med. **30**:977, 1933.

19. Elsberg, C. A.; Spotnitz, H., and Strongin, E. I.: Effect of Stimulation by Odorous Substances upon Amount of Secretion of Parotid Glands, J. Exper. Psychol. **27**:58, 1940.

20. Kohnstamm, O.: Der Nucleus salivatarius Chordae tympani, Neurol. Centralbl. **21**:848, 1902.

21. Yagita, K.: Untersuchungen über das Speichelzentrum, Anat. Anz. **35**:70, 1910.

histophysiologic investigations of Miller,[22] established that this group of nerve cells, which Kohnstamm called the nucleus salivatorius, runs from the sensory nucleus of the seventh nerve down to the anterior end of the nucleus ambiguus. The more posterior portion of this group of cells, the so-called nucleus salivatorius inferior (or posterior), sends secretory (parasympathetic) fibers to the homolateral parotid gland. There is no sharp division between the salivary nerve fibers carried in the seventh and in the ninth cranial nerve, and Reichert and Poth [23] have stated the opinion that the parotid glands in human beings receive their secretory fibers from both of these cranial nerves. The preganglionic fibers from the ninth nerve to the parotid gland traverse the tympanic cavity as Jacobsen's nerve and reach the otic ganglion with the small superficial petrosal nerve. Postganglionic fibers arise from the ganglion and reach the gland through the auriculotemporal nerve. The sympathetic nerve fibers of the parotid gland are derived from the cervical portion of the sympathetic system through the superior cervical ganglion and reach the gland as postganglionic fibers along the arteries to the parotid gland.

In the diencephalon, particularly in the hypothalamic centers which regulate control of visceral functions, there are groups of cells which are related to salivary activity. Müller [24] stated that stimulation of the subthalamic area results in secretion of saliva and tears. Papez [25] expressed the opinion that salivary reactions are mediated through the dorsomedial and ventromedial nuclei of the hypothalamus (small-celled nuclei). Stimulation of these areas reduces heart rate and increases salivation, tonus of the urinary bladder and intragastric pressure. These effects are stopped by atropine. The lateral and posterior hypothalamic area, which contains the larger motor-like cells, is said on stimulation to produce marked inhibition of gastrointestinal peristalsis, decreased salivation, increased blood pressure and reduced intragastric pressure, metabolic activity and heat production. Lesions in or destruction of these areas give results opposite to stimulation. From the foregoing observations it may be assumed that there is not only parasympathetic control exerted by certain subthalamic areas but sympathetic control as well. Sixty years ago Lépine and Bochefontaine [26] discovered that stimulation with an induction current of the cerebral cortex behind and below the sulcus

22. Miller, F. R.: On the Reactions of the Salivary Centers, Quart. J. Exper. Physiol. **6**:57, 1913.

23. Reichert, F. L., and Poth, E. J.: Pathways for the Secretory Fibers of the Salivary Glands in Man, Proc. Soc. Exper. Biol. & Med. **30**:973, 1933.

24. Müller, L. R.: Lebensnerven und Lebenstriebe, ed. 3, Berlin, Julius Springer, 1931, p. 180.

25. Papez, J. W.: Cerebral Mechanisms, J. Nerv. & Ment. Dis. **89**:145, 1939.

26. Lépine, R., and Bochefontaine, L.: L'influence de l'excitation du cerveau sur la sécrétion salivaire, Gaz. méd. de Paris **46**:332, 1875.

cruciatus in a dog produces secretion of saliva from the parotid glands, and this observation has been confirmed by many later investigations (Babkin 1938). Fulton, Kennard and Watts [27] gave Vogt and Brodman's area 6 aβ as a center which on stimulation produces salivation. In general, it is stated that the center for salivary reactions is in the premotor area near the area representing the face. Papez [25] stated the belief that this evidence gives only a fraction of the total picture and that the more important regions for autonomic representation in the cerebral cortex are to be found elsewhere, probably in the region of the gyrus cinguli and the hippocampus. The pyramidal and extrapyramidal fibers have been suggested as the connecting links with the lower centers (Spiegel and Hunsicker, 1936). However, these areas of the cortex are not to be regarded as ordinary "centers" for salivary secretion, for Tichomirov [28] revealed that the conditioned salivary reflexes did not disappear after extirpation of these areas in both hemispheres in a dog. This emphasizes Goldstein's [29] hypothesis that the "functional" center is not identical with the anatomic and that only "castastrophic" situations can lead to functional paralysis of an organ.

The afferent nerves of the parotid glands are carried in the glossopharyngeal, lingual, buccinator and palatine nerves and in the pharyngeal branch of the vagus.

Stimulation of the parasympathetic nerves leading to the parotid glands produces both a secretory and a vasodilator effect on these glands. The effects transmitted through the sympathetic nerves are of three types: "trophic," "motor" and "vasoconstrictor." Heidenhain [30] introduced the concept of the "trophic" effect of a glandular nerve, implying the conversion into soluble form and subsequent discharge of colloidal organic material stored in the secretory cells. This function of the glandular nerves is entirely distinct from their secretory function, by means of which the passage of water and salts from the blood through the secretory cells is regulated. Heidenhain [31] held that the trophic fibers are supplied to glands by the sympathetic nerves, while the secretory fibers originate chiefly from the parasympathetic system. Confirmation of this theory is found in the report that stimulation of the sympathetic fibers to a parotid gland (provided the parasympathetic

27. Fulton, J. F.; Kennard, M. A., and Watts, J. W.: Autonomic Representation in the Cerebral Cortex, Am. J. Physiol. **109**:37, 1934.

28. Tichomirov, N. P.: Thesis, St. Petersburg, 1906.

29. Goldstein, K.: The Organism, New York, American Book Company, 1939.

30. Heidenhain, R.: Ueber sekretorische und trophische Drüsennerven, Arch. f. d. ges. Physiol. **17**:1, 1878.

31. Heidenhain, R.: Beiträge zur Lehre von der Speichelabsonderung, Studien, des physiologischen Institutes zu Breslau, Leipzig, Breitkopf & Hörtel, 1868, pt. 4, p. 1.

fibers have not been stimulated shortly before and the tympanic nerve has been cut to prevent a reflex effect) produces no perceptible flow from the gland (Howell [32] and Best and Taylor [33]). It does produce, however, a striking change in the subsequent type of saliva secreted by the gland, the organic matter being often tenfold that obtained by stimulation of the parasympathetic fibers alone.

Some investigators in the field do not agree on this point (Babkin [34] and Baxter [35]), but they generalize about the secretory innervation of all the salivary glands and have not limited their discussions to the parotid glands. This is evident from Babkin's argument, in which he postulated that the parasympathetic nerve fibers innervate the mucous cells of the salivary glands while the sympathetic fibers produce changes in the serous cells. This obviously applies only to the mixed glands, because the parotid glands are, on the basis of the best authorities, completely serous glands. In addition, he based some of his statements on evidence accumulated by Rawlinson [36] in studies on cats, whose salivary reactions are known to be different from those of man. Various authors have suggested that the three pairs of large salivary glands respond normally to different stimuli, and Pavlov [37] supported this view.

The "motor" effect of the sympathetic nerves on a parotid gland consists of a contraction of the gland under sympathetic stimulation. This has been confirmed by Anrep and Khan.[38] Subsequent investigations showed that the contraction of the gland is not effected by muscular tissue but is probably brought about by the special contractile myoepithelial cells (Babkin and McKay [39]) lying between the membrana propria and the basal part of the cells.

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32. Howell, W. H.: A Textbook of Physiology, ed. 14, Philadelphia, W. B. Saunders Company, 1940.

33. Best, C. H., and Taylor, N. B.: Physiological Basis of Medical Practice, Baltimore, William Wood & Company, 1937.

34. Babkin, B. P.: (*a*) The Physiology of the Salivary Glands, Dental Science and Dental Arts, edited by Gordon, Philadelphia, Lea & Febiger, 1928, p. 219; (*b*) footnote 8.

35. Baxter, H.: The Influence of Section of the Cervical Sympathetic Nerve and Extirpation of the Superior Cervical Ganglion on the Composition of the Parotid Saliva in the Dog, Am. J. Physiol. **97**:668, 1931.

36. Rawlinson, H. E.: Cytological Changes After Autonomic and Adrenalin Stimulation of the Cat's Submaxillary Gland, Anat. Rec. **57**:289, 1933.

37. Pavlov, I. P.: The Work of the Digestive Glands, translated by W. H. Thompson, ed. 2, London, C. Griffin & Co., 1910, p. 32.

38. Anrep, G. V., and Khan, H. N.: The Metabolism of the Salivary Glands: V. The Process of Reconstruction of the Submaxillary Gland, J. Physiol. **58**:302, 1924.

39. Babkin, B. P., and MacKay, M. E.: Concerning the Motor Mechanism of the Salivary Glands, Am. J. Physiol. **91**:370, 1930.

The hormonal control of parotid activity is also a controversial subject. Cannon and his associates[40] demonstrated that stimulation of sympathetic fibers conveying impulses to smooth muscles of the vessels of the legs or of the splanchnic region produces sympathomimetic effects in many distant organs, including the salivary glands, by the liberation in the body of sympathin. This same substance is liberated by stimulation of the sympathetic fibers innervating the salivary glands (Cattel, Wolff and Clark[41]), and there is little doubt that this adrenergic agent transmits the impulses from the sympathetic nerve fibers to the gland cells. On the other hand, Sacks and Kim[42] stated that the secretory activity of the salivary glands is regulated exclusively by the nerves and that there is no specific hormonal mechanism for salivary secretion. The preponderance of evidence points to the functional interdependence of the vegetative nervous system and the endocrine glands, but as yet this relationship obviously is unclarified. Hoskins[43] remarked about this: "In the meantime it is not wise to be misled into a feeling of false security by premature schemata purporting to set forth these relationships so that he who runs may read."

To summarize from the preceding discussion the points most important in evaluating and explaining the results of this study, it may be said that the preponderance of evidence shows that the secretory activity of the parotid glands is controlled primarily by the parasympathetic nervous system and that the sympathetic system has no effect on rate. However, before being willing to say to any extent that what is measured with the rate of parotid secretion is primarily parasympathetic function, I should have to convince myself that the sympathetic innervation had no primary effect on this rate. In an attempt to show this small doses of epinephrine hydrochloride (0.1 cc.) of a 1 : 1,000 solution were given hypodermically to 3 children (ages 5, 8 and 9 years) after their characteristic rates had been established. This was enough to raise the blood pressure 30 to 50 mm. of mercury, to increase the pulse rate 50 to 70 beats and to produce moderate evidence of vasoconstriction (pallor, etc.). However, no great change in parotid secretory

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40. Cannon, W. B., and Bacq, Z. M.: Studies on the Conditions of Activity in Endocrine Organs: XXVI. A Hormone Produced by Sympathetic Action of Smooth Muscle, Am. J. Physiol. **96**:392, 1931. Cannon, W. B., and Rosenblueth, A.: Autonomic Neuro-Effector Systems, New York, The Macmillan Company, 1937. Studies on Conditions of Activity in Endocrine Organs: XXIX. Sympathin E and Sympathin I, Am. J. Physiol. **104**:557, 1933. Cannon, W. B.: Chemical Mediators of Autonomic Nerve Impulses, Science **78**:43, 1933.

41. Cattel, M.; Wolff, H. G., and Clark, D.: The Liberation of Adrenergic and Cholinergic Substances in the Submaxillary Gland, Am. J. Physiol. **109**:375, 1934.

42. Sacks, J., and Kim, M. S.: On the Non-Existence of a Hormone for Salivary Secretion, Proc. Soc. Exper. Biol. & Med. **27**:193, 1929.

43. Hoskins, R. G., and Lee, M. O.: The Internal Secretions and the Autonomic Nervous System, A. Research Nerv. & Ment. Dis., Proc. (1928) **9**:361, 1930.

rate was noted. In 2 instances it went up slightly for two minutes ("motor" effect?); in the third, it went down after a slight rise. The rates in all subjects remained within the same range they had been in before administration of the drug. However, when a larger dose of epinephrine hydrochloride solution was given fifteen minutes later, a dose large enough to produce symptoms of alarm and mild shock in the subjects (0.5 cc.), the rate definitely went down. (For a discussion of the effect see the section on pharmacologic reactions in part IV.)

Further corroboration of the thesis that it is primarily the effect of the parasympathetic nerve on the glands which is measured by the use of the parotid secretory rate was found clinically during a study of 2 children who were hospitalized at Babies Hospital for obvious sympathetic imbalances. These children had fluctuating high blood pressures, unstable pulse rates, marked vasomotor changes in the skin, dermographia, etc. Their parotid secretory rates in each instance were definitely within the normal range and did not vary with the changes in the other signs and symptoms as might be expected if this rate were a sympathetically determined function.

IV. PHYSIOLOGIC AND PSYCHOLOGIC ASPECTS OF UNSTIMULATED, OR RESTING, PAROTID SECRETION

The physiologic and psychologic factors affecting the rate of secretion of a resting parotid gland are important in this problem because they must all be taken into consideration in actual performance of the tests and evaluation of the results. In general, it may be said that the end results of most conditions affecting the rate may be related to the protective, moistening, cleansing and digestive functions of the parotid secretions. Before these factors are examined, however, it would not be amiss to review what is known concerning this rate of secretion while the glands are at rest.

There is considerable difference of opinion in the literature concerning the occurrence of a continuous secretion of saliva in human beings during rest. The results reported before Lashley's disk came into use differed in both fact and theory. Since then a great deal has been learned about the existence of this rate and the factors which control it. Since the observations before 1916 were not evaluated in terms of these factors, it is best to leave them out of this discussion with only enough mention of them to show the previous disagreement. For instance, Mitscherlich,[1] Ordenstein,[7] Stoney-Butler,[2] Küss [3] and Krasnogorski [6] reported unactivated parotid secretions in their subjects with fistulas or in their cannulated subjects. Zebrowski [4] and Brunacci [44] took the opposite stand on the question.

44. Brunacci, B.: Sulla funzione secretoria della parotida nell'uomo; nota prima; influenza della qualità dello stimolo sulle proprietà fisicochimiche della saliva parotidea, Arch. di fisiol. **8**:421, 1910.

Following Lashley, Morris and Jersey,[45] Allen,[46] Birukov,[47] Krasnogorski,[17] Winsor[48] and Strongin,[49] all noted an unstimulated resting secretion. Babkin in 1914 argued against the presence of such a secretion, but in his later reviews on the subject [50] he reversed his stand somewhat, leaving the question open. However, he cited evidence against such a rate from experiments on animals, which since have been repeated in the light of newer knowledge. For instance, while Mangold [51] and Pavlov [52] (1927) failed to find spontaneous, continuous secretion in dogs and observed it only in ruminant animals, Gooreev [53] and Liddell (1938) have found a small amount of such secretion in dogs. Lashley [54] stated that the resting secretion "may be reflex in nature, since there is probably a constant stimulation of the mucosa of the digestive tract." Winsor [55] interpreted his findings on resting secretions to indicate a glandular tonicity analogous to that of muscular tonus.

For convenience the chief conditions affecting the parotid activity may be grouped into five categories: local effects, general conditions, factors related to the nervous system, gastrointestinal conditions and pharmacologic reactions. Some of the factors could be fitted into more than one group, and often they were arbitrarily placed in one or another category for convenience in presentation.

Local Effects.—1. The question of whether or not the disks themselves might activate the glands was considered by Lashley [54] and later

45. Morris, J. L., and Jersey, V.: Chemical Constituents of Saliva as Indices of Glandular Activity, J. Biol. Chem. **56**:31, 1923.

46. Allen, F.: The Secretory Activity of the Parotid Gland, Quart. J. Exper. Physiol. **19**:336, 1929.

47. Birukov, D. A.: Unconditioned Salivary Reflexes in Man, Rostov-on-Don, U. S. S. R., State Publishing House, 1935.

48. Winsor, A. L.: Conditions Affecting Human Parotid Secretion, J. Exper. Psychol. **11**:355, 1928.

49. Strongin, E. I., and Hinsie, L. E.: Parotid Secretory Rate in Schizophrenic Patients, J. Nerv. & Ment. Dis. **87**:715, 1938.

50. Babkin, B. P.: Die äussere Sekretion der Verdauungsdrüsen, ed. 2, Berlin, Julius Springer, 1928; footnote 34 *a*.

51. Mangold, E.: Handbuch der Ernährung und des Stoffwechsels der landwirtschaftlichen Nutztiere als Grundlagen der Fütterungslehre, Berlin, Julius Springer, 1929, vol. 2, p. 113.

52. Pavlov, I. P.: Conditioned Reflexes: An Investigation of the Physiological Activity of the Cerebral Cortex, translated and edited by G. V. Anrep, New York, Oxford University Press, 1927.

53. Gooreev, T. T.: The Periodic Activity of the Salivary Glands, Conditioned Reflexes, Collected Papers of the Psychoneurological Institute of the Ukraine Kharkov, 1932, p. 187.

54. Lashley, K. S.: Reflex Secretion of the Human Parotid Gland, J. Exper. Psychol. **1**:461, 1916.

55. Winsor, A. L.: Observations on the Nature and Mechanism of Secretory Inhibition, Psychol. Rev. **37**:399, 1930.

by Winsor.[48] They demonstrated that the activating influence of the disks themselves is negligible.

2. Muscular exercise expressed in terms of local changes about the oral cavity, i. e. swallowing and similar activities, such as movements of the mouth, sucking on the disks, yawning and belching, causes a slight rise in rate. On the other hand, with intense more generalized muscular exercise a slight increase in rate is shortly followed by a moderate drop (Nekrassov and Khranilova [56]).

3. Some of the Russian investigators have described a so-called "water reflex"; i. e., water placed into the mouth causes a flow of parotid saliva (Birukov [47]). However, this has been found to be more of a local temperature effect. With temperatures above and below that of the body there is an increase of flow. Water at 37.5 C. in the mouth has no observable effect on the secretory rate (Brunacci [44]).

4. Local irritations, such as painful dental conditions or oral lesions, cause an increase in rate. This is most likely an expression of the protective function of saliva in the mouth.

5. The fatigue of the parotid glands themselves or the exhaustion of the secretory supply was often considered to be a possible disturbing factor in experimental work. However, Lashley [13] recorded little change in secretions when the glands were activated for ten minutes. Winsor [57] reported no marked diminution after fifty minutes of chewing. Heidenhain [30] (with weak induction shocks) obtained a secretory activity which kept up for "hours." Apparently the parotid glands are relatively indefatigable.

6. The state of the glands at the time of the test is important in the test, not from the point of view of previous activity, which as has just been shown has little effect, but in regard to inactivity. Winsor [57] found that "within certain limits the longer the rest periods preceding excitation, the more rapid the subsequent rate of secretion." This "reservoir" effect may account for the increased secretory flow on awakening from sleep.

General Conditions.—1. Careful studies made by Korchin [12] on the effect of weight, height, pulse rate and blood pressure on the rate of parotid secretion showed no correlation between them. Certainly the investigation of somatic components has thrown no light on the question of the wide range of individual differences. Apropos of the studies on blood pressure, it may be noted in passing that the pressure of

56. Nekrassov, P. A., and Khranilova, N. V.: The Influence of Physical Work on the Unconditioned Salivary Reflex in Man, Arkh. biol. Nauk **35**:593, 1934.

57. Winsor, A. L.: The Effect of Mental Effort on Parotid Secretion, Am. J. Psychol. **43**:434, 1931.

the parotid secretion is consistently higher than blood pressure and is apparently not related to it.

2. Dehydration is of course a pronounced factor in reduction of rate, since the salivary output is to a great extent dependent on the water balance of the organism. Gregersen and his co-workers [58] emphasized the influence of thirst on the rate of salivary secretion, and Winsor [59] reported the cutting down of parotid secretions by 50 per cent in one hour when dehydrating agents were used. The normal secretory rate was quickly restored when liquid was ingested. Precautions may be taken in this regard by using the McClure-Aldrich technic of evaluating roughly the water balance of the body by a cutaneous test (part II).

3. Infectious diseases, especially rabies and smallpox, often cause an increase more marked than that accounted for by higher temperatures. In parotitis the secretions are lowered (Krasnogorski [17]).

4. Position of the body is important in the test. Standing diminishes the rate of secretion, and it is possibly this factor which explains Pavlov's reports [60] that no "inactivated" secretions were found in the dogs (which were standing when tested) used in his experiments. Lying down will similarly cause a reduction in secretion. Sitting comfortably is the position of choice for the patient.

Factors Related to the Nervous System.—1. Sleep has a definite inhibitory effect on rate of parotid secretion. This effect is roughly proportional to the depth of sleep. The investigator can usually tell when a subject has fallen asleep in the middle of an experiment because of the change in rate. In hypnosis too (Jenness and Hackman [16]) there is a similar reduction in rate, varying with the depth of hypnosis.

In coma of the hypoglycemic type (during treatment with insulin) it was found that there is a sharp rise in rate with the onset of the stuporous state (Strongin, Hinsie and Harris, 1938). However, while the patients slept, as they often do during the earlier stages of an insulin treatment, the rate showed a drop. There is, therefore, a differential point, detected by the use of this apparatus, between coma and sleep, and certainly the technic should be valuable in future research on sleep itself.

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58. Gregersen, M. I.: Conditions Affecting the Daily Water Intake of Dogs as Registered Continuously by a Potometer, Am. J. Physiol. **102**:344, 1932. Gregersen, M. I., and Bullock, L. T.: Observations on Thirst in Man in Relation to Changes in Salivary Flow and Plasma Volume, ibid. **105**:39, 1933. Gregersen, M. I., and Cannon, W. B.: The Effect of Extirpation of the Salivary Glands on the Water Intake of Dogs While Panting, ibid. **102**:336, 1932.

59. Winsor, A. L.: The Effect of Dehydration on Parotid Secretion, Am. J. Psychol. **42**:602, 1930.

60. Pavlov, I. P.: Lectures on Conditioned Reflexes, translated by W. H. Gantt, New York, International Publishers, 1928; footnote 52.

Closely related to this question is that of anesthesia. While no studies have been made on human beings, Robbins [61] reported of dogs: "All of the anaesthetics cause a cessation of salivary secretion during anaesthesia by depressing the secretory center." He also found that ether and chloroform cause an increased secretion in dogs during induction.

2. Emotional factors have long been known to have definite effects on the body secretions. As far as the secretory rate of the parotid glands is concerned, it has been determined that minor emotional reactions cause a slight increase in secretion while more intense emotional experiences, such as excitement, fear, etc., after causing a transitory rise in output produce an inhibition (Wittkower and Pilz; Korchin and Winsor [12]). Farr [62] pointed out the same phenomenon in gastric secretion. Disgust, embarrassment, pain and erotic emotions have also been shown to have a depressing effect on the rate of parotid secretion, while pleasurable sensations may increase the rate slightly. Although Lashley [13] concluded that "there is no direct reflex to olfactory, ordinary visual, auditory or tactile stimulation," subsequent investigators have tended to disagree with him.[19]

3. The development of conditional salivary reflexes in human beings is another controversial area. Richter and Wada [14] have denied that such conditioning is possible, while Lashley,[54] Smirnov [5] and Krasnogorski [17] among others have said that it is possible. Winsor and Bayne [63] suggested that the conditioned reflexes set up in human beings depend on a multiplicity of intrinsic and extrinsic factors. For example, the reflexes set up with food seem to depend largely on the state of hunger of the subject. Certainly the conditioning process, even in children, is a much more complicated one than in dogs, and the reflexes, when and if established, are not stable. Their effect on secretion in any case is transitory, lasting at the most a few minutes. Therefore, if any such process was unwittingly set up by the test procedure, perhaps by some such factor as the subject's knowledge that he was to get a lollypop after each test, its effect would be only short lived and would not be reflected to any great extent in the results of the tests, which extended over a period averaging twenty to twenty-five minutes.

4. It has been determined that there is usually in human beings a dominance of one parotid gland which is consistent for any given person.

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61. Robbins, B. H.: Effect of Various Anesthetics on Salivary Secretion, J. Pharmacol. & Exper. Therap. **54**:426, 1935.

62. Farr, C. B.: Effect of Emotion on Gastric Secretion, Baltimore, Wilkins & Wilkins Company, 1931, p. 217.

63. Winsor, A. L., and Bayne, T. L.: Unconditioned Salivary Responses in Man, Am. J. Psychol. **41**:271, 1929.

Korchin [12] has found that males are predominantly left glanded and females right glanded. This correlates well with Pende's [64] observation that males are usually left glanded over their whole bodies (the left testicle larger than the right), while females are predominantly right glanded (right breast and right lobe of thyroid larger, etc.). This has no correlation with handedness, footedness or eyedness, however. In my studies on children I have not found any consistent sex-determined glandedness. It has been suggested as possible that when sex hormones are changed from their even balance of prepubescence to a male or female preponderance after puberty, glandedness could also conceivably change. This is a highly speculative question and is of only academic interest now.

5. Mental work, concentration on a task or a problem, causes in most subjects a decrease in rate. I have been able to confirm Birukov's [47] and Winsor's [57] observations on this point, except that on rare occasions in my experiments a child working on a problem during a test period showed no change or even a slight rise in secretion. Possibly this is caused by concomitant movements of the mouth and tongue, as suggested by Lashley. It is interesting in this connection to note that when a series of 10 mongolian idiots under 12 years of age were given a picture game to work on during part of the test the rate consistently increased. I am unable to explain this paradoxic reaction.

6. In schizophrenia and depressions of the manic-depressive type in adults, rates of parotid secretion show decided changes (Strongin and Hinsie [49]). While persons with early schizophrenia had little change in rate from normal, the more deteriorated subjects showed an acceleration in rate. This increase was proportional to the degree of regression. This will be considered later in the light of some of my data. In manic-depressive depression there is a complete or almost complete inhibition of rate, which is so consistent that it has been considered as an aid in differential diagnosis between this type of depression and others.

7. Lesions of the central nervous system should, if my outline of the neuroanatomy of the parotid gland is valid, produce changes in rate. It has been found by Lashley,[65] by Elsberg and Spotnitz (unpublished data) and by me in my own investigations that this is true. Lashley's observations were made on patients with fully developed hemiparesis or hemiplegia. He concluded: "The greater secretion in every case appeared on the side showing the more thorough involvement in the paralysis." Elsberg and Spotnitz found unilateral changes in rate with

64. Pende, N.: Constitutional Inadequacies, Philadelphia, Lea & Febiger, 1928.

65. Lashley, K. S.: Changes in the Amount of Salivary Secretion Associated with Cerebral Lesions, Am. J. Physiol. **43**:62, 1917.

certain types of tumors of the brain in adults. These and Lashley's observations are true for children.

Gastrointestinal Conditions.—Gastrointestinal conditions have decided effects on the secretory rate of the parotid glands at rest. To summarize the considerable literature on this point, it may be said that hunger and fasting inhibit the parotid secretion while satiation causes its enhancement. Therefore, it is important to perform tests about two hours after mealtime, to avoid both the postprandial rise and the preprandial decline.

Hisada [66] in 1930 showed that distention of the stomach brings about an increase in rate of parotid secretion (possibly a reflex response via the vagus). He also found that subnormal gastric temperature depresses the rate while supernormal temperatures result in an increased flow.

The only observations on the effects of diet on secretory rate in human beings were those of Ordenstein,[7] who found no correlation between type of food ingested and rate of flow.

As would be expected, the parotid glands respond most readily to gustatory stimuli, and it is on this fact that most of the conditioning experiments were based in the past.

Pharmacologic Reactions.—The usual reactions to drugs which affect the parasympathetic and sympathetic nerves hold true for the parotid glands. Often paradoxic effects of the use of these drugs are found in children, which has discouraged me from extended pharmacologic experiments. This reversal of effect has been explained in many ways. Langley [67] thought of it before the experiments of Fröhlich and Loewi [68] as due to the action of a sympathetic drug on parasympathetic end apparatus or vice versa. He also spoke of the reversal as showing that the action is determined by the condition of the tissue and is not an expression of normal neural action. Epstein [69] theorized that a balanced central nervous system reacts to a stimulus in a constant way. In other words, the condition of the central nervous system may determine the result of the reaction. Another explanation depends on Cannon's homeostatic and Jelliffe's homeokinetic concepts, according to which the different reactions can be explained by the shifting of calcium and potassium ions in the cells, by the general condition of the receptive substance, by the organs of internal secretion and by conscious and

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66. Hisada, K.: Ueber die reflektorische Speichelsekretion durch Magenaufblähung, Arch. f. d. ges. Physiol. **224**:249, 1930.

67. Langley, J. N.: The Salivary Glands, in Schefer: Text-Book of Physiology, London, Y. J. Pentland, 1898, vol. 1, p. 475.

68. Fröhlich, A., and Loewi, O.: Ueber vasokonstriktorische Fasern in der Chorda tympani, Zentralbl. f. Physiol. **20**:229, 1906; Arch. f. exper. Path. u. Pharmakol. **59**:64, 1908.

69. Epstein, A.: The Reflexes of the Vegetative Nervous System, Leningrad, U. S. S. R., State Publishing House, 1925.

unconscious psychic factors. The method of administration and the dosage do not often seem to be essential factors. The most important factor which Sachs[70] has been able to arrive at in explaining these seemingly paradoxic reactions to a drug is the previous state of excitability and tonus of the sympathetic or parasympathetic system. He stated that "when the excitability reaches its maximum, a further stimulation of the same nerve will accordingly lead to a paradoxical reaction." For example, a single injection of a pilocarpine salt increases the secretory rate of a child's parotid gland, while a second injection fifteen minutes later, instead of increasing the rate further, will cause the enhanced rate to decrease somewhat.

It is important to know that in the evaluation of the foregoing physiologic and psychologic factors on the rate of parotid secretion in children it has been noticed that while any one factor may increase or decrease the rate the degree of change is seldom sufficient to change a child's reaction from the range that is characteristic of his age group. (This is discussed more fully later in this study.)

V. RATE OF PAROTID SECRETION IN NORMAL CHILDREN

The establishment of normal standards for the secretory rate of the parotid glands in children, essential for the evaluation of the findings in abnormal states, was undertaken with rigid standards for normality of the subjects. The children included in this group were known to be normal physically, to have no known personality deviations and to be making good social and school adjustments. When possible, children were selected who had been subjected to a period of stress and had reacted without disturbance to the trying situation. Such children were made available through one of the large foundling hospitals, where detailed records are kept from early childhood for most children. Many of the subjects were picked from the Normal Child Development Study at the Babies Hospital, where they had been followed regularly, often daily, with many technics since they were 10 days of age. These subjects were particularly valuable in the younger age groups (under 4 years), in which the cooperation and other attributes needed in this procedure would not ordinarily be present in youngsters not used to having proceedings of all types carried out on them. Although it was later apparent that there is no correlation between the intelligence quotient and the parotid secretory rate, all the children used were of average intelligence.

A total of 51 children were selected thus, ranging in age from 3 to 14 years. Nine age groups were established, the subjects from 11 to 14 years being grouped as one for convenience and because of similarity

70. Sachs, W.: The Vegetative Nervous System, London, Cassell & Co., Ltd., 1936.

in rate. Until proper disks are devised, the study of the secretory rate of the unstimulated, or resting, parotid gland in children under 3 years of age will be unsatisfactory for mechanical reasons. In the younger age groups at the start age in months was used, but the variations in rate from child to child in any age group were too gross for such fine differentiation. The results will be found in the table.

Figure 2 graphically shows the relationship of parotid salivary rate to age. The extremely high rates are apparently normally confined to the younger age groups (3 to 5 years). From 5 to 7 years of age the rates are much lower, being one-half to one-fourth that of the earlier age ranges. From 7 to 14 years there is a gradual, slightly uneven drop to levels which approach in early puberty those of normal adults (0.02 to 0.12 cc. per five minutes; average, 0.07 cc. per five minutes). These figures do not confirm Lashley's statement that the rates of children are somewhat lower than those of adults.

Secretory Rate of the Parotid Gland of Normal Children

Age, Years	Number of Children	Mean Rate in 0.01 Cc. per Five Minutes	Range
3-4	5	74.2	59-98
4-5	6	52.6	35-70
5-6	5	24.1	19-30
6-7	7	15.8	6-26
7-8	6	12.8	4-22
8-9	8	15.7	3-22
9-10	4	8.9	5-14
10-11	4	11.2	9-12
11-14	6	10.6	4-18

This curve, of course, is incomplete because of the absence of adequate data from birth till 3 years of age. The trend in the rates if continued in the pattern they seem to follow in the earlier years would be to increase as one goes down the age scale, and it would finally be infinity at birth. Therefore, it is obvious that at some point below 3 years of age there must be a leveling off of the rate of secretion. Probably from birth to a few months of age the rate is low. Clinically an infant certainly has an abundance of saliva by 5 to 6 months of age, when the drooling which accompanies the eruption of teeth becomes noticeable. In normal full term infants saliva has been found in the mouth before food is taken.[71] Only small amounts are found at birth, but it is definitely present, as shown by the infant's ability to digest starch. In fact, Nicory [72] has demonstrated the presence of ptyalin in the parotid gland one and one-half months before birth. Mayer has presented some evi-

71. Growth and Development of the Child: II. Anatomy and Physiology, White House Conference on Child Health and Protection, New York, Century Company, 1933.

72. Nicory, C.: Salivary Secretions in Infants, Biochem. J. **16**:387, 1922.

dence [73] that more is secreted by older infants than by younger ones. I have been able to confirm the presence of parotid secretion in newborn babies and in infants up to 4 months of age. The conditions under which saliva from the parotid glands must necessarily be collected in these infants (with jaw retractor in place, etc.) would invalidate any conclusions as to resting rate.

The curves representing the rapid drop in rate of secretion in the younger age groups and the gradual decrease thereafter would seem to

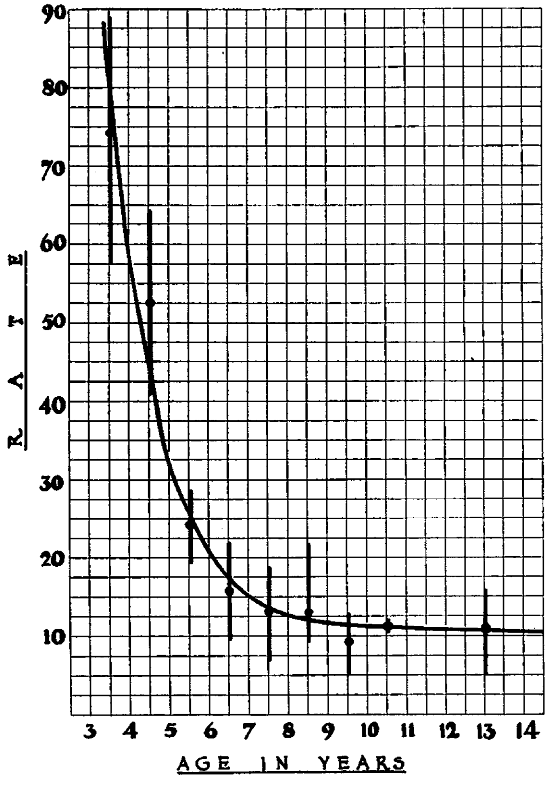

Fig. 2.—Rate of secretion of the parotid glands of normal children. The rate is expressed in terms of 0.01 cc. per five minutes. A-11; k-6.85 per cent per month; the vertical lines indicate the median zone, in which two thirds of the values would be expected to fall, i. e., σ.

represent a function of growth and development. They appear similar to the growth curves obtained in following the development of other body functions, such as heart rate (the slowing of which with age is to

73. Mayer, W. B.: Comparison of Amylase Concentration in the Saliva of Infants and Adults, Bull. Johns Hopkins Hosp. **44**:242, 1929.

some extent a parasympathetic function). One may be allowed to think, therefore, that one is measuring with this curve maturation of the mechanism by which the parotid secretion is mediated, that is, the autonomic nervous system and more particularly the parasympathetic nervous system. However, it cannot be maturation in an anatomic sense that is measured here, because the parasympathetic fibers, which act as the secretory innervation (part III) of the parotid glands, are myelinated at birth. Rather it may be thought of as a maturation of function which becomes evident as the higher centers which affect salivary functioning become sufficiently developed with increasing age to exert their effects on the rate of flow. These midbrain and cortical areas (part III), the presence of which is only sketchily known, may be thought of as directing an inhibitory action on the relatively high rate which would result from the unmodified medullary activity alone.

The few investigators of function of the autonomic nervous system in children have agreed that the child is essentially vagotonic (Pende, Sachs, Eppinger and Hess), becoming gradually less so as he approaches puberty. If one thinks of the rate of parotid secretion as a measure of parasympathetic function, this concept is borne out by my results.

Since in a speculative way the development of cortical activity was mentioned as a possible factor in causing the drop of rate with advancing age in children, it is interesting to compare the curves prepared by Weinbach at Babies Hospital from data compiled by Smith [74] on the development of alpha rhythms in the brain waves of children. When the frequency of alpha waves per second is plotted against age in years, it is found that from a low of 2 waves per second under 1 year of age there is a rapid rise in frequency till about 5 years of age, when a point between 7 and 8 waves per second is reached. From then on there is a more gradual, somewhat uneven rise until after 12 years of age the frequency reaches a point definitely above 9 cycles per second. It will be seen in comparing my figures with these that the increase in alpha rhythms with age is accompanied by a coincident drop in parotid secretory rate. The periods of rapid and then gradual change parallel each other in the measurement of the two functions. In fact, if the curve for change in parotid secretory rate with age is turned upside down, it matches exactly the curve for change in Berger rhythm with age. One has, therefore, an objective measure of the maturation of cortical function which closely parallels the objective measure of the maturation of parotid function, which adds evidence to the hypothesis that it is the development of the influence of the cortex on the lower centers which causes the drop in rate with age.

74. Smith, J. R.: The Electroencephalogram During Normal Infancy and Childhood, J. Genet. Psychol. **53**:455, 1938.

In order to determine the statistical validity of the data presented here, the results were subjected to an analysis of variance according to the method of Fisher.[75] The sources, or variables, included in this analysis were age, sex, restlessness of the subject, minute to minute variation in rate and interindividual differences. Each five minute period was treated separately, and then all the variables were checked over a fifteen minute period. The only significant factor found was the change in rate with age. Restlessness was an apparently somewhat significant factor, but when this too was subjected individually to an analysis of variance it was found to mean only that the restless subjects in any age group were those with the higher rates in that age group and that restlessness had no influence on the change of rate with age.

COMMENT

It has been concluded from parts III and V that there are relationships between the cortex, midbrain and bulbar centers for salivary activity. I have also felt with Foerster [76] that the newborn child is a being in whom only the subcortical centers, thalamus and pallidum, are functioning. It has been postulated that as the child's higher centers mature and exert their inhibitory influence on the lower ones, this increasing ability to inhibit is reflected in the changes in rate of parotid secretion with age. It is an accepted theory that this inhibitory effect of the higher centers is widespread over all subcortical functions. It may be thought of as also having an influence on behavior, which is only a resultant of many factors controlled by the nervous system. This influence on behavior must be reflected at any given age level by the balance between the subcortical and the cortical influences.

With this in mind consider the case of a 10 year old child who cannot apply a check element to his activities, shows evidence of disorganized behavior and has a consistently high rate of parotid secretion, the same as that of a normal 3 year old child. It may be suspected that in such a child the behavior is a reflection of the same failure or delay in maturation represented by the parotid secretory rate. Certainly there is even more reason to suspect that this is true when it is found that children who have normal secretory rates seem to have a better chance to clear up personality disturbances that they may encounter than other youngsters who present similar behavior problems but have abnormal parotid secretory rates.[77]

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75. Fisher, R. A.: Statistical Methods for Research Workers, ed. 5, Oliver & Boyd, London, 1934.

76. Foerster, O.: Antidrome Leitung im sensibeln Nerven, Klin. Wchnschr. **59**:453, 1922.

77. Lourie, R. S.; Barrera, S. E., and Strongin, E. I.: Autonomic Nervous System Function in Children with Behavior Problems as Measured by the Parotid Secretory Rate, Am. J. Psychiat. **99**:419, 1942.

In other pathologic states there is likewise evidence for this correlation between type of behavior and rate of salivary secretion. It is generally agreed that the chronic impulsiveness, aggressiveness and overactivity of the classic postencephalitic patient represent a loss of ability to apply a check to behavior. Witness also in many such patients the drooling of saliva from the mouth. This represents more strictly a regression to a lower level of maturation rather than a delay of maturation.

Another striking example of the relation between regressive disturbances in conduct and parotid activity is to be found in the study of the rate of parotid secretion in schizophrenia by Strongin and Hinsie.[49] Their studies now take on new implications from the present observations on normal children. They reported that the deeper the deterioration, the higher goes the rate. In other words, as the schizophrenic patient regresses to a more infantile level, to the point where he is smearing feces and returning to primtive grasping and sucking reflexes, the rate of parotid secretion too goes back to infantile levels.

The results found by the same authors in depressions of the manic-depressive type may be thought of in the same terms. If, as has been suggested, depressions of this type are the result of the higher brain centers applying an excessive degree of inhibition on lower centers, it is also significant that there is during these depressed states a complete inhibition of activity of the resting parotid glands.

Another point of view from which the results in this study may be evaluated is that of constitutional medicine. Following the terminology of Pende,[64] those children who have a tendency to retain high, or infantile (immature), salivary secretory rates could be thought of as showing hypoevolutism. (Their condition may also be thought of as representing the somatic component of a psychosomatic whole.)

It is interesting to examine Krasnogorski's [78] classification of physiologic types of children in light of the evidence from these results. He has postulated:

1. The central (well balanced) type, in whom the normal infracortical processes are well regulated by the strong cortical activity. These children should and do have normal parotid secretory rates.

2. The subcortical type, in whom the infracortical processes have the upper hand over the cortical influences. In these children the parotid secretory rates are high.

3. The cortical type, in whom the balance is shifted toward a predominance of cortical activity over subcortical activity (anxiety states?). These have comparatively low secretory rates.

78. Krasnogorski, N.: Physiology of Cerebral Activity in Children as a New Subject of Pediatric Investigation, Am. J. Dis. Child. **46**:473 (Sept.) 1933.

4. The anergic (hypodynamic) type, in whom both the cerebral cortex and subcortical areas are equally hypoexcitable. These children may have any type of rate, depending on superimposed conditions, but it is usually low. Krasnogorski felt that this is the type of child in whom a psychosis develops.

No correlation has been found in this study between rate of parotid secretion and severity of symptoms.

I should like to point out the other directions which the study of the parotid secretory rate in children has taken.

There has become evident in the course of these experiments the existence of a salivolacrimal reflex; with crying there is an increase in parotid secretory rate, and on unilateral olfactory stimulation there is not only an increase in rate of homolateral parotid activity but of lacrimation as well.

In organic neurologic disorders there are indications that the salivary rate may be of some aid in localization of lesions of the brain, tumors, etc.

In differential diagnosis of types of hyperkinetic children the parotid rate has proved of value in picking out children in whom the hyperkinesis may be on the basis of a developmental delay.

In the field of mental deficiency, it has been found that mongolian idiots have normal rates but have the paradoxic rise of rate on concentration that was mentioned earlier. Cretins when not receiving thyroid have low rates and when receiving thyroid have high rates. Familial mental defectives have no characteristic rate but may vary as much as does the population in general, except that possibly they have a higher incidence of increased rates on the whole. All microcephalic children have extremely high rates.

CONCLUSION

The first known use of the salivary secretions as a test is that described by Cannon as having been prevalent centuries ago in certain oriental countries, where the ordeal of rice placed in the mouth of an accused person was used as an indication of fear and therefore of guilt. However, it is only comparatively recently that it was realized how the study of the secretory activity of the salivary glands could be utilized as an aid in physiologic investigations. Especially in the fields of pediatrics and psychiatry it offers the investigator an objective laboratory measure which may be used in the study of psychosomatic reactions. The parotid gland in particular is valuable from this point of view because it is made easily accessible with the aid of a simple laboratory device.

I have gone into considerable detail to describe the technic used in this study of the parotid secretory activity because it was felt to be worth while to record this method, especially since it differs in some fundamental ways from that used heretofore with children.

One fact which has become increasingly evident in researches into the literature on this subject is the considerable use made of translating the results of animal experiments into terms applicable to human beings. This dangerous anthropomorphizing is to blame for much of the confusion and disagreement prevalent among the investigators in the field of salivary activity.

Drs. Nolan D. C. Lewis, S. E. Barrera and Rustin McIntosh, of the College of Physicians and Surgeons, assisted in the general preparations of this study. Dr. A. A. Weech, of Babies Hospital, assisted in formulating and evaluating the problem here investigated; Dr. Joseph Zubin, of Psychiatric Institute, and A. P. Weinbach, of Babies Hospital, rendered assistance in the statistical analyses. Drs. E. I. Strongin and B. Korchin placed their experience in the field of parotid gland reactions at my disposal.

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